Remarks

Claims 19-88 are pending. Claims 19, 53, and 57 have been amended to more clearly claim embodiments that Applicants regard as the invention. Specifically, the claims have been amended to specify that the antibodies or portions thereof of claims 19, 53, and 57 are either human, humanized, or chimeric. These claims previously recited human antibodies or portions thereof. Support for humanized and chimeric antibodies is found in the specification at least at page 38, first paragraph and in the originally filed claims. No new matter has been introduced.

I. Withdrawal of claims 44-52, 80-88, and 151-161

Claims 44-52, 80-88, and 151-161 have been withdrawn by the Examiner as directed to non-elected subject matter. Applicants note that claims 151-161 were previously canceled in their response dated October 21, 2002. Pending claims 44-52 and 80-88 are directed to methods of detecting CSG10 protein using the antibodies of claim 19 or claim 57, and were part of Group VIII in the Examiner's restriction requirement. The remaining pending claims are directed to antibodies and are from elected Group III. Applicants have previously requested rejoinder of the method claims of Group VIII, which includes pending claims 44-52 and 80-88. *See* Applicant's Response of October 21, 2002. Accordingly, Applicants again respectfully request that if any of the antibody claims are found allowable, then claims 44-52 and 80-88 be rejoined and examined for patentability.

II. Rejections under 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 19-43 and 53-79 under 35 U.S.C § 112, first paragraph for alleged lack of enablement. *See,* Paper No.9, pages 2-4. Specifically, the Examiner asserts at page 2 of the Office Action:

> [T]he specification, while being enabling for applying the colon specific gene protein to produce monoclonal antibody, does not reasonably provide enablement for producing any isolated human protein which binds to a protein selected from the group consisting of 1 to 323 of SEQ ID NO:16.

The Examiner further states that "the specification provides guidance only with regard to apply the colon specific gene protein to produce monoclonal antibody (See pg. 43, example 2)". Paper No. 9 at page 3, lines 12-13.

Applicants respectfully disagree. The disclosures in the specification, in the context of the knowledge in the art at the time of filing, enable a wide variety of antibodies, including human, humanized, and chimeric antibodies. While Example 2 does teach the production of monoclonal antibodies as stated by the Examiner, this example is not limiting. The specification specifically states: "The present invention will be further described with reference to the following examples; however, it is to be understood that the present invention is not limited to such examples." Specification at page 39, lines 19-22. In addition to monoclonal antibodies, the specification teaches that a variety of antibodies and antibody deriviatives can be prepared against colon specific gene protein:

> The polypeptides, their fragments or other derivatives, or analogs thereof, or cells expressing them can be used as an immunogen to produce antibodies thereto. These antibodies can be, for example, polyclonal or monoclonal antibodies. The present invention also includes chimeric, single chain, and humanized antibodies, as well as Fab fragments, or the product of an Fab expression library. Various procedures known in the art may be used for the production of such antibodies and fragments.

Specification at page 38, lines 1-9. In the subsequent paragraphs the specification teaches the production of polyclonal, monoclonal, and single chain antibodies, as well as the production of antibodies in transgenic animals and the labeling of antibodies. Specification at page 38, line 10 through page 39, line 18.

Furthermore, it is well understood that enablement is provided not only by Applicants' specification, but also by what was known in the art at the time of filing. "The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." *United States v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed Cir. 1988). Moreover, "[a] patent need not teach, and preferably omits, what is well known in the art." M.P.E.P. 2164.01, citing *In re Buchner*, 929 F.2d 660, 661 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452 (Fed. Cir. 1984).

In the present case, it would have been routine at Applicants' priority date for the skilled artisan to produce a variety of human antibodies, not just monoclonal human antibodies, based on widely known, published, and readily available techniques together with Applicants' disclosures. For example, technology to produce fully human antibodies in transgenic animals was published at least as early as 1994. *See, e.g.*, Lonberg et al., Nature 368:856-859 (1994); abstract provided as Exhibit A. Lonberg et al. described transgenic mice expressing human IgM, IgG, and Ig kappa in the absence of mouse IgM or Ig kappa. The mice were shown to undergo V(D)J joining, heavy-chain class switching, and somatic mutation, resulting in a repertoire of human immunoglobulins. Lonberg et al. immunized the mice with human proteins. Thus, the skilled artisan could clearly have used the Lonberg et al. transgenic mice to produce both human polyclonal and human monoclonal antibodies. This is merely one example of technology known at the time of Applicants' priority date which would have allowed a person of skill in the art to make a variety of human antibodies to colon specific gene protein without undue experimentation.

Furthermore, technology for making chimeric antibodies, including humanized antibodies, was also well known at the time of Applicants' priority date. *See, e.g.*, Winter et al., Nature 349:293-299 (1991); provided as Exhibit B. Winter et al. described chimeric and humanized antibodies *inter alia* at page 293, right column, and in Figure 2. Winter et al. also describe a variety of different portions of antibodies (*see, e.g.*, Fig. 2).

Finally, in response to the previous Office Action, Paper No. 6, Applicants argued that the "human antibody or portion thereof" of Applicants' claims were neither anticipated nor obvious over Oda et al., (J. Biol. Chem. 268:5929-5939 (1993)), who disclosed a polyclonal rabbit antibody to rat RI-H protein, which is 77% identical to Applicants' SEQ ID NO:16. Applicants wish to hereby restate for the present amended claims that Oda et al., either alone or in the various combinations with other references as presented in Paper No. 6, fails to teach or suggest the human, humanized, or chimeric antibody of the present claims. Oda et al. merely teach a rabbit polyclonal antibody used in a Western blot to detect a different protein with 77% amino acid sequence identity.

Applicants assert that the disclosures and references discussed above demonstrate that the present claims directed to a "human, humanized, or chimeric antibody or portion thereof" are enabled as to their full scope. Therefore, the withdrawal of this rejection is respectfully requested.

III. Compliance with 37 C.F.R. §§ 1.821(a)(1) and 1.821(a)(2)

The instant application allegedly is not in compliance with 37 C.F.R. §§ 1.821(a)(1) and 1.821(a)(2) for lack of a sequence listing in either paper or computer readable form (CRF) and lack of sequence identifiers in the specification. *See* Paper No. 9 at page 4 and Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicants respectfully disagree. The Preliminary Amendment submitted by Applicants on November 19, 2001 added appropriate sequence identifiers to the specification and directed the entry of the Sequence Listing previously filed in earlier Application Serial No. 08/469,667. A paper copy of that sequence listing was included with the Preliminary Amendment, and a statement under C.F.R. § 1.821(e) was also included, which requested the use of the CRF from the earlier application. A copy of the stamped post card from Applicants' November 19, 2001 filing is submitted herewith as Exhibit C. Thus, the instant specification is indeed in compliance with C.F.R. §§ 1.821(a)(1) and 1.821(a)(2). Nonetheless, as a courtesy to the Examiner, Applicants submit herewith copies of the Sequence Listing, in paper and computer readable forms, filed in Application Serial No. 08/469,667. The copies submitted herewith are identical to those filed in earlier Application Serial No. 08/469,667, whose entry in the present case was already requested in the Preliminary Amendment of November 19, 2001. Thus, in view of the above, Applicants respectfully submit that the instant application fully complies with the requirements set forth in C.F.R. § 1.821.

Conclusion

In view of the amendments and remarks above, Applicants believe that this application is in condition for allowance. If in the opinion of the Examiner a telephone conference would expedite prosecution, the undersigned can be reached at the telephone number indicated below.

If there are any fees due in connection with the filing of this paper, please charge the fees to Deposit Account No. 08-3425.

Respectfully submitted,

Dated: 15 April 2003

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Guo-Liang Yu

Attorney Docket No.: PF160D2

Application No.: 09/988,292

Group Art Unit: 1637

Filed: November 19, 2001

Examiner: J. Tung

For: Colon Specific Genes and Proteins

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

The claims have been amended as follows:

19. (Twice Amended) An isolated human, humanized, or chimeric antibody or portion thereof that specifically binds to a protein selected from the group consisting of:

    (a) a protein whose sequence consists of amino acid residues 1 to 323 of SEQ ID NO:16;

    (b) a protein consisting of a fragment of SEQ ID NO:16, wherein said fragment comprises at least 30 contiguous amino acid residues of SEQ ID NO:16; and

    (c) a protein consisting of a fragment of SEQ ID NO:16, wherein said fragment comprises at least 50 contiguous amino acid residues of SEQ ID NO:16.

53. (Twice Amended) An isolated human, humanized, or chimeric antibody or portion thereof produced by immunizing an animal with a protein selected from the group consisting of:

    (a) a protein whose sequence comprises amino acid residues 1 to 323 of SEQ ID NO:16;

    (b) a protein whose sequence comprises at least 30 contiguous amino acid residues of SEQ ID NO:16; and

    (c) a protein whose sequence comprises at least 50 contiguous amino acid residues of SEQ ID NO:16,

wherein said antibody or portion thereof specifically binds to the amino acid sequence of SEQ ID NO:16.

57. (Once Amended) ~~An isolated~~ The antibody or portion thereof of claim 19 that specifically binds ~~to a protein whose sequence consists of amino acid residues 1 to 323 of SEQ ID NO:16~~ protein (a).